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May 26, 2004

Michael O. Leavitt, Administrator
U.S. Environmental Protection Agency
Ariel Rios Building, 1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on the HPV Test Plan for Benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts

Dear Administrator Leavitt:

The following comments on ACC HERTG's test plan for the chemical Benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

ACC HERTG submitted its test plan on December 17, 2003, for the chemical Benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts (CAS No. 114959-46-5). This compound, also referred to as calcium alkyl salicylates, is used as a detergent additive in gasoline and diesel engine oils, aids in keeping soot in suspension to minimize sludge formation, and as a base for neutralization of acids. ACC HERTG has submitted a test plan that lacks significant detail; although it acknowledges that testing will be carried out to fulfill the SIDS endpoints for subchronic toxicity, reproductive toxicity, developmental toxicity, and chromosomal aberration, there is no mention of the OECD protocols it plans to use to evaluate these endpoints. At the very least, we would like to ensure that if testing is conducted, protocols employ the minimum number of animals.

To its credit, ACC HERTG did make use of available data on two formulations of Benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts: a 43% formulation referred to as AI-43 and a 28% formulation referred to as AI-28. Existing toxicity data for these formulations were used to bridge data gaps for ecotoxicity and acute toxicity and mutagenicity in mammals. This approach is not only a scientifically valid analysis of a chemical's toxicity and adequate for a screening level program, it is also consistent with EPA's stated goal of maximizing the use of existing data in order to limit additional animal testing.

If ACC HERTG plans to conduct further animal tests on this chemical, we ask that the combined repeated dose/reproduction/developmental study (OECD 422) be conducted.

EPA accepts this combined screen to meet all three SIDS endpoints and uses the minimum number of animals versus conducting each study separately. In addition, we request that the *in vitro* rodent embryonic stem cell test (EST) be conducted in parallel. Although conducting these tests in parallel will not spare any animals at this point in time, it would assist with building the database for this non-animal method. The EST has recently become commercially available in the U.S., and was validated by the European Centre for the Validation of Alternative Methods last year. The Centre's Scientific Advisory Committee concluded that the EST was ready to be considered for regulatory purposes (Genschow 2002). We have already written the ACC on this matter and are awaiting a response. This would be a good opportunity for ACC HERTG to work with EPA and the animal welfare community to incorporate this validated non-animal test into the HPV program.

With regard to genetic toxicity of calcium alkyl salicylates, testing for chromosomal aberration should be conducted using an *in vitro* method, per EPA guidance, should ACC HERTG wish to investigate this endpoint. Thank you for your attention to these comments; we would appreciate receiving a direct response to our specific concerns with this test plan. I may be reached at 202-686-2210, ext. 327, or via e-mail at *meven@pcrm.org*.

Sincerely,

Megha Even, M.S.
Research Analyst

Chad B. Sandusky, Ph.D.
Director of Research

References

Genschow, E., *et al.*, "The ECVAM international validation study on *in vitro* embryotoxicity tests: Results of the definitive phase and evaluation of prediction models", *Alternatives to Laboratory Animals* 30: 151-76, 2002.